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67

| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.   | CONFIRMATION NO. |
|---|-------------|----------------------|-----------------------|------------------|
| 10/080,435  | 02/22/2002  | Mark G. Erlander     | 485772003300          | 8216             |
| 20350   | 7590        | 10/04/2005           | EXAMINER              |                  |
| TOWNSEND AND TOWNSEND AND CREW, LLP<br>TWO EMBARCADERO CENTER<br>EIGHTH FLOOR<br>SAN FRANCISCO, CA 94111-3834 |             |                      | CHUNDURU, SURYAPRABHA |                  |
|   |             |                      | ART UNIT              | PAPER NUMBER     |
|   |             |                      | 1637                  |                  |
| DATE MAILED: 10/04/2005   |             |                      |                       |                  |

Please find below and/or attached an Office communication concerning this application or proceeding.

| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|------------------------------|------------------------|---------------------|--|
|                              | 10/080,435             | ERLANDER ET AL.     |  |
| Examiner                     | Art Unit               |                     |  |
| Suryaprabha Chunduru         | 1637                   |                     |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 08 September 2005.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 1-21 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-21 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on 22 February 2002 is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date

4)  Interview Summary (PTO-113)  
Paper No(s)/Mail Date. 9116 (05)

5)  Notice of Informal Patent Application (PTO-152)

6)  Other: \_\_\_\_\_.

**DETAILED ACTION**

1. Upon reconsideration of applicants' request for reconsideration of the finality of the last Office action, the finality of that action is withdrawn herein.

***Status of the Application***

2. Claims 1-21 are pending. All arguments have been thoroughly reviewed and deemed persuasive. This action is made Non-Final.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 provides for the use of a plurality of agents, attached to a plurality of different nucleic acid molecules simultaneously, to detect a plurality of ligands, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 8-9 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 1-8, 10-19, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ornstein et al. (Clin Cancer Res., Vol. 6, page 353-356, 2000) in view of Eberwine et al. (6,255,060).

Ornstein et al. teach a method of claims 1-2, and 4 for detecting the presence of a ligand in a cell or tissue, comprising;

obtaining a tissue sample, staining said tissue sample to identify cells of interest (see page 353, col. 2, lines 1-4 under materials and methods section);  
capturing or isolating said cells of interest (see capture by laser capture microdissection (LCM)) (see page 353, col. 2, line 5-6, under materials and methods section, page 354, col. 1, line 8);

detecting said ligand (PSA) in the captured cells (see page 354, col. 1, paragraph 1, indicating detection of PSA ligand in the LCM procured cells).

With regard to claim 3, Ornstein et al. teach that said sample is a tissue section (see page 353, col. 2, line 1-2 under materials and methods section);

With regard to claim 6-7, Ornstein et al. teach that said staining is by histochemical staining and capturing by LCM (see page 353, col. 2, line 3-6, indicating H & E stain and LCM for capturing);

With regard to claim 10, Orstein et al. teach that said sample is prostate tissue (see page 353, col. 2, line 1-2 under materials and methods section);

With regard to claim 11, Orstein et al. teach that said ligand is prostate specific ligand (PSA) see page 354, col. 1, paragraph 1, indicating detection of PSA ligand in the LCM procured cells);

With regard to claim 12, Orstein et al. teach said capturing involves two types of cells (normal and malignant cells) (see page 353, col. 2, paragraph 2 under introduction subheading);

However, Ornstein et al. did not teach contacting said tissue sample with a binding agent (antibody) attached to a detectable nucleic acid.

Eberwine et al. teach a method 1-2, 4-5, 12-19, 21, for detecting a ligand in a cell by immuno PCR, (semi-quantitative) PCR wherein said method comprises use of antibody-conjugated to a nucleic acid to detect said ligand (see col. 2, line 43-55). Eberwine et al. also teach (i) said nucleic acid comprises a promoter (see col. 2, line 48-55); (ii) said promoter is a T7 promoter (see col. 4, line 44-47); (iii) said detection comprises contacting said promoter with T7 polymerase and identifying transcription initiated from said T7 promoter said detection is carried

out by PCR amplification (see col. 4, line 41-60); (iv) quantitation of presence of ligand (see col. 2, line 53-57) (v) plurality of ligands wherein said plurality of ligands comprises two forms of a polypeptide (phosphorylated and unphosphorylated forms) (see col. 5, line 12-34); (vi) detecting the ligand in single cell (col. 7, line 5-6).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detecting a ligand as taught by Ornstein et al. in a manner of as taught by Eberwine et al. with a step of including antibody conjugated to a nucleic acid sequence comprising a promoter for the purpose of increasing the sensitivity of the assay in detecting a ligand in cells sample. One skilled in the art would be motivated to combine the method as disclosed by Ornstein et al. in a manner taught by Eberwine et al. because Eberwine et al. explicitly taught that the method permits the detection of small amounts of protein-antibody complexes by incorporating the sensitivity and accuracy of promoter driven transcription or amplification using antibody conjugated T7 promoter driven cDNA sequence (see col. 4, line 41-44). An ordinary artisan would have a reasonable expectation of success that inclusion of the step of inclusion of T7 promoter driven cDNA sequence amplification would result in detecting small amounts of a ligand in a single cell with more sensitive and accurate detection of said ligand and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

B. Claims 9, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ornstein et al. (Clin Cancer Res., Vol. 6, page 353-356, 2000) in view of Eberwine et al. (6,255,060) as applied to claims 1-8, 10-19, 21 above, and further in view of Oku et al. (USPN. 5,789,165).

Ornstein et al. in view of Eberwine et al. teach a method for detecting a ligand in a cell or tissue sample as discussed above in section 5A.

Neither Ornstein et al. nor Eberwine et al. teach that the plurality of agents as antibodies and use of microarry for detecting the transcription products.

Oku et al. teach a method for detecting plurality of ligands using plurality of binding agents (antibodies) attached to different nucleic acid molecules (see col. 4, line 9-21). Oku et al. also teach that the plurality of ligands are detected by an array of solid phases comprising ligands comprising nucleic acid molecules capable of binding said ligand by base pair complementarity (see col. 6, line 37-47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect the presence of plurality of ligands by combining the method of Ornstein et al. in view of Eberwine et al. in a manner taught by Oku et al. by using the plurality of binding agents attached to different nucleic acid molecules and detecting the ligands by the use of an array comprising base complementarity nucleic acid sequences to achieve expected benefit of developing a multiplex method of detecting Plurality of ligands in a single assay format because Oku et al. taught that use of plurality of binding agents in a single reagent provides detection of plurality of ligands in a single assay reagent (see col. 4, line 5-12). An ordinary practitioner would have been motivated to combine the method of for detecting the presence of a ligand in a cell as taught by Ornstein et al. in view of Eberwine et al. with the step of multiple binding agents for the purpose of analysis of multiple ligands in a cell sample. The ordinary artisan would have a reasonable expectation of success that inclusion of multiple binding agents taught by Oku et al. would result in an increase in a high-throughput assay for detecting multiple

ligands and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

***Response to arguments:***

6. With regard to the rejections made in the previous office action under 35 USC 103(a), Applicants' arguments are fully considered and all the rejections under 35 USC 103(a) are withdrawn herein in view of the persuasive arguments.

***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

Art Unit: 1637

system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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